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PARATHION TOXICITY IN PERINATAL RATS EXPOSED IN UTERO

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SUMMARY

Adult pregnant female rats were exposed to subchronic doses of parathion throughout gestation and lactation. Their offspring were examined for possible toxicological effects. This study found that several physiological parameters were affected. Female perinates exhibited a significant reduction in plasma cholinesterase (pseudo ChE) activity. Plasma renin activity was reduced with increased dose of parathion in both male and female perinates. Heart rate, QRS complex duration, S-T and P-R intervals were all reduced in the perinates. The results of this study indicated that physiological function can be altered by organophsophate exposure at levels lower than those required to show pseudo ChE inhibition.

INTRODUCTION

Placental transfer of organophosphorous compounds has been documented in sheep [1] and in mice [2]. The work of Gagne and Bodeur [3] suggests that weanlings may be more susceptible to parathion than adults. Additionally, male rats appear to exhibit a greater resistance to phosphorothioates than do female rats [4].

The mode of action of organophosphate insecticides is mainly through the inhibition of the enzyme AChE, an effect which has been observed in mammals [1,2,5]. Toxic manifestations of these compounds include miosis, lacrimations, muscle fasciculations, atrial fibrillation, conduction block, and initial tachycardia and increased blood pressure, followed by bradycardia and decreased blood pressure in the later stages of poisoning [6]. Surprisingly little research has been conducted with respect to the effects of parathion on cardiac function and blood pressure regulation. It is the intent of this study

*This research was done in partial fulfillment of the requirements for the Master of Science degree in Physiology at North Carolina State University, Raleigh, NC 27607 (U.S.A.).
Abbreviations: AChE, acetylcholinesterase; ChE, cholinesterase.

to examine the effects of parathion on EKGs and plasma renin activity, using cholinesterase activity as an index of poisoning in perinatal rats exposed in utero and during lactation.

METHODS

Adult time pregnant rats of the CD strain (random bred albino) were used (Charles River Breeding Laboratory, Wilmington, Mass.). Food and water were provided ad libitum with a light:dark cycle of 12:12.

Parathion (obtained from the EPA Pesticide Repository, RTP, NC) was administered in peanut oil by oral gavage at doses of 0.01, 0.10 and 1.00 mg/kg/day. The compound was administered from day 2 of gestation through day 15 of the lactation period. Peanut oil alone was administered to a control group.

On day 24 post partum ten perinates at each dose level were examined for possible toxicity. RBC (true ChE) and plasma (pseudo ChE) cholinesterase activities were measured by a pH stat method using acetylcholine perchlorate as the substrate [7]. Plasma renin activity was measured by radioimmunoassay (Malinckrodt Nuclear, St. Louis, Mo.). Perinates were anesthetized with sodium pentobarbital (45 mg/kg) and electrocardiograms recorded with reference electrodes placed subcutaneously in both forelimbs, using the left leg as ground [8].

Analysis of variance was performed with the Statistical Analysis System 72 [9]. The level of statistical significance was chosen as $P < 0.05$.

TABLE I

ANALYSIS OF TRUE AND PSEUDO CHOLINESTERASE DETERMINED FROM 24-DAY-OLD PERINATAL RATS EXPOSED TO PARATHION

Dose (mg/kg)	Male	Female
(A) *True ChE*		
Control	1.56 ± 0.09[a]	1.67 ± 0.14
0.01	1.25 ± 0.08	1.67 ± 0.16
0.10	1.66 ± 0.16	1.55 ± 0.20
1.00	1.67 ± 0.15	1.86 ± 0.17
(B) *Pseudo ChE*		
Control	0.58 ± 0.06	0.84 ± 0.02
0.01	0.67 ± 0.03	0.70 ± 0.03[b]
0.10	0.62 ± 0.01	0.61 ± 0.02[b]
1.00	0.71 ± 0.02	0.61 ± 0.03[b]

[a]Mean ± SEM expressed as μmol of acetylcholine perchlorate hydrolyzed per min per ml of plasma or packed cells.
[b]Significant compared to control ($P < 0.05$).

RESULTS

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Table I. True
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was decreased
(Table II).
The effect
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parathion.

TABLE II

ELECTROCAR
FEMALE PERI

Dose (mg/kg/da

Control
0.01
0.10
1.00

[a]Mean ± SEM.
[b]Significant cor

TABLE III

PLASMA RENI
EXPOSED TO

Dose (mg/kg/da

Control
0.01
0.10
1.00

[a]Mean ± SEM e
[b]Significant cor

RESULTS

The effect of parathion on true and pseudo ChE activities is shown in Table I. True and pseudo ChE activities were unaffected in the male perinates. Female perinates showed a significant decrease in pseudo ChE activity at doses of parathion of 0.01 mg/kg and above, while true ChE activity was unaffected in the female perinates.

The rate of atrial depolarization (P-R interval) and ventricular repolarization (S-T interval) both showed a significant decrease at parathion doses of 0.01 mg/kg and above. Ventricular depolarization (QRS complex duration) was decreased, with statistical significance noted at the 1.00 mg/kg dose level (Table II).

The effect of parathion on plasma renin activity is described in Table III. Male perinates showed a reduction in plasma renin activity, with statistical significance noted at the 0.10 and 1.00 mg/kg dose levels. Female perinates showed the same response, with significance seen at all three dose levels of parathion.

TABLE II

ELECTROCARDIOGRAPHIC DATA OBTAINED FROM 24-DAY-OLD MALE AND FEMALE PERINATAL RATS EXPOSED TO PARATHION

Dose (mg/kg/day)	Interval (expressed in msec)			Heart rate (beats/min)
	QRS Duration	S-T	P-R	
Control	110 ± 6[a]	70 ± 10	70 ± 7	428 ± 8
0.01	100 ± 10	40 ± 1[b]	40 ± 1[b]	392 ± 26
0.10	90 ± 10	20 ± 4[b]	30 ± 2[b]	411 ± 20
1.00	40 ± 10[b]	10 ± 3[b]	20 ± 1[b]	408 ± 21

[a]Mean ± SEM.
[b]Significant compared to control ($P < 0.05$).

TABLE III

PLASMA RENIN ACTIVITY OBTAINED FROM 24-DAY-OLD PERINATAL RATS EXPOSED TO PARATHION

Dose (mg/kg/day)	Sex	
	Male	Female
Control	2.70 ± 0.12[a]	4.84 ± 0.34
0.01	2.32 ± 0.08	1.96 ± 0.22[b]
0.10	1.82 ± 0.37[b]	1.62 ± 0.35[b]
1.00	1.52 ± 0.13[b]	0.66 ± 0.32[b]

[a]Mean ± SEM expressed as ng/ml/h.
[b]Significant compared to control ($P < 0.05$).

DISCUSSION

The AChE data obtained from this study are consistent with the literature demonstrating a greater female susceptibility and/or greater male resistance to organophosphate poisoning [10]. Female perinatal rats showed a significant reduction in pseudo ChE at doses of parathion of 0.01 mg/kg and above.

The important point made by this study is that in perinatal rats exposed to parathion in utero and through day 15 of lactation altered EKG patterns were seen. This study found that perinatal rats exhibited altered EKG patterns at a dose of parathion lower than that necessary to cause pseudo ChE inhibition.

Plasma renin activity also showed significant changes in perinates at doses of parathion which did not cause plasma cholinesterase inhibition.

This study suggests that the use of cholinesterase activity as the major criterion for OP poisoning may be an oversimplification and that cardiovascular damage may be a consequence of parathion exposure.

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